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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1637	10

DATE MAILED: 01/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,063	ROTHSCHILD ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *4-6,12,13,15,21-25,30-35 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-11,14,16-20,26-29,36-38 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-29 and 36-40, and Species III – MseI restriction site, SEQ ID NO:s 12 and 13 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that no separate search is required for the non-elected species. This is not found persuasive because each sequence will require a separate search using separate resources of the STIC computer system. Further, each species will require separate consideration with regard to the prior art.

Therefore, claims 30-35 drawn to a nonelected group and claims 4-6, 12, 13, 15, 21-25 and 39 drawn to nonelected species are withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Sequence Rules

2. The current case fails to meet sequence rules outlined in 37 C.F.R. 1.821-1.825. In particular, there are sequences on page 38 and 41-43 which are present but which are not associated with SEQ ID Nos. Also, the paper copy and CRF submitted only include SEQ ID Nos: 1-7, and do not include SEQ ID Nos: 8-13, and therefore, fail to include the elected species. The elected sequences were manually searched by the examiner (by hand entry of the sequences into the search system).

Full compliance with the Sequence Rules in response to this action is required, or the response will be non-responsive.

Specification

3. The disclosure is objected to because of the following informalities:

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 7 of specification, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01..

Appropriate correction is required.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3, 7-11, 14, 16-20, 26-29, 36-38 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which comprise prolactin receptor polymorphisms which are not disclosed in the specification. The genus includes an enormous number of polymorphisms for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named four polymorphisms for which data is provided demonstrating an association with the phenotypic trait, litter size. Thus, applicant has express possession of only four particular polymorphisms, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed which would permit selection of sequences as polymorphisms. Even in the narrower dependent claims, such as claim 7, where MseI is required, no specific polymorphism is named. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations of associating a polymorphism with litter size is provided. Further, these claims expressly encompass all the different possible allelic variants including insertions, deletion, substitutions and transversions at thousands of different sites. No written description of alleles, of upstream or downstream regions containing additional sequence, which are associated with any phenotype are described in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition in claim 1 of a polymorphism associated with litter size which lacks any specific structure, is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the four specific polymorphisms, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "a polymorphism in the prolactin receptor gene", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise prolactin receptor polymorphisms. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-3, 7-11, 14, 16-20, 26-29, 36-38 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some polymorphisms in the porcine prolactin receptor such as the Alu polymorphism, does not reasonably provide enablement for all polymorphisms including the MseI polymorphism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method of screening animals for polymorphisms in the prolactin receptor gene which are associated with increased litter size. The invention is is the class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims are broadly drawn to encompass a method of screening for any polymorphism in the prolactin receptor gene. Even the narrow claim 7 is drawn to any polymorphism which can be detected by the use of the MseI restriction enzyme. The method broadly encompasses the use of the method in any type of mammalian patient. Further, the animals undergoing the screening may contain any of a number of complicating variables, since the background genotype with regard to other genes may play significant roles in the effect on litter sizes.

Quantity of Experimenation

The quantity of experimentation in this area is very large since there is significant variability in the effects of polymorphisms on phenotypes such as litter size. Screening each possible polymorphism in the prolactin receptor gene represents an inventive, unpredictable and difficult undertaking in itself. As shown in the results on page 46, over 1500 litters were analyzed involving literally hundreds of pigs. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The specification demonstrates the unpredictability of this invention, since the P values identified by the specification for the association of the MseI SNP with litter size are 0.2 and 0.3. As Thisted et al notes (See http://www.stat.uchicago.edu/~thisted) "It has become scientific convention to say that p-values exceeding 0.05 (one in twenty) just aren't strong enough to be the sole evidence that two treatments being studied really differ in their effect (see page 5)". Thus, by scientific convention, the data presented for the Mse1 SNP on page 46 of the specification fails to demonstrate a statistically significant effect. It is highly unpredictable whether the SNP is, in fact, associated with the increased litter size. Unlike the Alu1 polymorphism, shown on page 36, where there is a P value below 0.05, the Mse1 polymorphism fails to show a significant effect. The factor of unpredictability weighs against the enablement of the claims.

Working Examples

The specification has a working example where an Alu polymorphism is clearly associated with litter size.

Guidance in the Specification.

The specification, while suggesting an association between the MseI SNP and litter size, did not provide sufficience evidence to demonstrate the association.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability and the teaching that the P values are insufficient are opposed to enablement of the invention (see Thisted above). The specification provides one with no written description or guidance that leads one to a reliable method where an MseI polymorphism is associated with litter size. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Further the specification does not provide guidance to overcome art and specification recognized problems in the use of polymorphisms as prognostic of litter size as broadly claimed. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the specific polymorphism at issue and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue

experimentation for one of skill in the art to perform the method of the claim as broadly written.

Double Patenting

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-3, 8-11, 16-20, 26-29, 36-38 and 40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 5,935,784 in view of Rothschild et al (U.S. Patent 5,374,526).

Claim 3 of U.S. Patent No. 5,935,784 teaches a method of screening pigs to determine those more likely to produce larger litters comprising: obtaining a DNA sample from a pig ; and assaying for the presence of a genotype characterized by a polymorphic Alu I site in the 3' region of the pig prolactin receptor gene, said genotype being one which is associated with increased litter size.

The species of claim 3 anticipates the more generic claim 1 of the current application which is drawn to any polymorphism associated with litter size.

Claim 3 of U.S. Patent No. 5,935,784 does not teach the use of the various detection methodologies such as RFLP analysis

Rothschild teaches methodologies of detection including RFLP (column 5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine claim 3 of U.S. Patent No. 5,935,784 with the methods and gene of Rothschild since Rothschild states "Thus, the markers will be

selection tools in breeding programs to develop lines and breeds that produce litters containing a larger number of offspring (column 2, lines 55-57)". An ordinary practitioner would have been motivated to identify such litter associated genes to increase litter size and thereby save money in pig breeding.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers

for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

January 3, 2003